



GAU 1633

PATENT
Attorney Docket No.: BIV-044.01
(21459-4401)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Miao et al.)
Serial No.: 08/900,220) Group Art Unit: 1633
Filed: July 24, 1997) Examiner: Wilson, M.
Title: Method of Treating Dopaminergic)
and GABA-nergic Disorders)

CERTIFICATE MAILING UNDER 37 C.F.R. §1.8(a)

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Sir:

Submitted herewith on Form PTO-1449 is a list of references known to Applicants and/or their Attorney/ Agent in compliance with the requirements of 37 CFR 1.56. A copy of each reference listed is also being submitted. Since this Information Disclosure Statement is being submitted before the mailing date of the first Office Action on the merits, no fee is due.

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached Form 1449.

This submission does not represent that a search has been made or that no better art exists. Nor does it constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim

in the application and Applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of such documents.

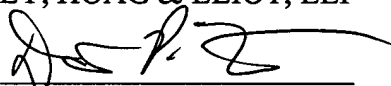
Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with this submission, please charge the fee to our Deposit Account, No. 06-1448.

Respectfully submitted,

FOLEY, HOAG & ELIOT, LLP

By:



David P. Halstead, Ph. D.

Reg. No. 44, 735

Agent for Applicants

Dated: 6/14/00
Foley, Hoag & Eliot, LLP
One Post Office Square
Boston, MA 02109
Voice: (617) 832-1000
Facsimile: (617) 832-7000

Form PTO-1449	Docket Number (Optional) BIV-044.01(21459-4401)	Application Number 08/900,220
INFORMATION DISCLOSURE CITATION IN AN APPLICATION (Use several sheets if necessary)		
Applicant Miao et al.		Group Art Unit 1633
Filing Date July 24, 1997		

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	KV 5, 759, 811	06/02/98	Epstein et al.	435	69.1	11/13/96
	KW 5, 223, 408	06/29/93	Goeddel et al.	435	69.3	07/11/91
	KX 4, 456, 687	06/26/84	Howard Green	435	241	12/01/80
	KY 5, 789, 543	08/04/98	Ingham et al.	530	350	12/30/93
	KZ 5, 844, 079	12/01/98	Ingham et al.	530	350	12/14/94
	LA 5, 585, 087	12/17/96	Lustig et al.	424	9.2	06/08/94
	LB 5, 837, 538	11/17/98	Scott et al.	435	325	10/06/95
	LC 5, 747, 507	05/05/98	Ikegaki et al.	514	312	08/10/93
	LD 5,643, 915	07/01/97	Andrulis, Jr. et al.	514	279	06/06/95
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FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation	
						YES	NO
	LF WO 90/02809	3/22/90	PCT	C 12P	21/00		
	LG WO 92/15679	9/17/92	PCT	C 12N	15/10		
	LH WO 94/28016	12/0894	PCT	C 07K	13/00		
	LI WO 95/23223	08/31/95	PCT	C 12N	15/00		
	LJ WO 96/ 09806	04/04/96	PCT				
	LK WO 96/11260	04/18/96	PCT	C 12N	5/00		
	LL WO 96/16668	06/06/96	PCT	A 61K	38/17		
	LM WO 96/17924	06/13/96	PCT	C 12N			
	LN WO 97/11095	03/27/97	PCT	C 07K	14/475		
	LO WO 97/45541	12/04/97	PCT	C 12N	15/12		
	LP WO 98/12326	03/26/98	PCT	C 12N	15/12		
	LQ WO 98/14475	04/09/98	PCT	C 07K	14/47		
	LR WO 98/21227	05/22/98	PCT	C 07H	21/04		
	LS WO 98/30234	07/16/98	PCT	A 61K	38/18		
	LT WO 98/30576	07/16/98	PCT	C 07K	1/100		
	LU WO 98/35020	08/13/98	PCT	C 12N	5/00		
	LV WO 99/00117	01/07/99	PCT	A 61K	31/00		
	LW WO 99/00403	01/07/99	PCT	C 07H	21/02		

LX	WO 99/01468	01/14/99	PCT	C 07K			
LY	WO 99/10004	03/04/99	PCT	A 61K	38/00		
LZ	WO 99/04775	02/04/99	PCT	A 61K	31/00		
MA	EP 0187 371 A2 ✓	07/16/86	European Patent Application				
MB	EP 0249 873 A2 ✓	06/10/87	European Patent Application				
MC	EP 0879888 A2 ✓	11/25/98	European Patent Application	C 12N	15/12		
MD	EP 0874048 A2 ✓	10/28/98	European Patent Application	C 12N	15/12		
ME	JP 63 08 81 12		Japan				
MF	JP 02 27 36 10		Japan				
MG	JP 04 30 55 28		Japan				

OTHER DOCUMENTS

(Including Author, Title, Date, Pertinent Pages, Etc.)

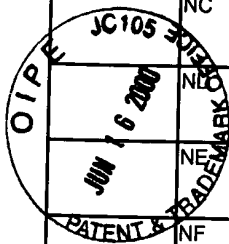
MH	Anderson, R. et al., "Maintenance of ZPA signaling in cultured mouse limb bud cells", <i>Devel.</i> <u>117</u> :1421-1433 (1993).						
MI	Angier, N., "Biologists find key genes that shape patterning of embryos", <i>New York Times</i> , Jan. 11, 1994, C-1.						
MJ	Basler, K. and G. Struhl, "Compartment boundaries and the control of <i>Drosophila</i> limb pattern by Hedgehog protein", <i>Nature</i> <u>368</u> :208-214 (1994).						
MK	Basler, K. et al., "Control of cell pattern in the neural tube: Regulation of cell differentiation by <i>dorsalin-1</i> , a novel TGF β family member", <i>Cell</i> <u>73</u> :687-702 (1993).						
ML	Bass, S. et al., "Hormone phage: An enrichment method for variant proteins with altered binding properties", <i>PROTEINS: Structure, Function, and Genetics</i> <u>8</u> :309-314 (1990).						
MM	Bejsovec, A. and E. Wieschaus, "Segment polarity gene interactions modulate epidermal patterning in <i>Drosophila</i> embryos", <i>Development</i> <u>119</u> :501-517 (1993).						
MN	Bienz, M., "Homeotic genes and positional signalling in the <i>Drosophila</i> viscera", <i>TIG</i> <u>10</u> :22-26 (Jan. 1994).						
MO	Bitgood, M. and A. McMahon, "Hedgehog and Bmp genes are coexpressed at many diverse sites of cell-cell interaction in the mouse embryo", <i>Dev. Biol.</i> <u>172</u> (1):126-138 (1995).						
MP	Blair, S. S., "Hedgehog digs up an old friend", <i>Nature</i> , <u>373</u> :656-657 (23 Feb. 1995).						
MQ	Brand-Saberi, B. et al., "The ventralizing effect of the notochord on somite differentiation in chick embryos", <i>Anat. Embryol.</i> <u>188</u> :239-245 (1993).						
MR	Brookes, J., "We may not have a morphogen", <i>Nature</i> <u>350</u> :15 (1991).						
MS	Bumcrot, D. A. et al., "Proteolytic processing yields two secreted forms of sonic hedgehog", <i>Mol. Cell. Biol.</i> <u>15</u> (4):2294-2303 (April 1995).						
MT	Bumcrot, D. A. and A. McMahon, "Sonic hedgehog: Making the gradient", <i>Chem. Biol.</i> <u>3</u> (1):13-16 (Jan 1996).						
MU	Bumcrot, D. A. and A. McMahon, "Somite differentiation. Sonic signals somites", <i>Curr. Biol.</i> <u>5</u> (6):612-614 (June 1995).						
MV	Charité, J. et al., "Ectopic expression of <i>Hoxb-8</i> causes duplication of the ZPA in the forelimb and homeotic transformation of axial structures", <i>Cell</i> <u>78</u> :589-601 (1994).						
MW	Coffman, et al., "Xotch, the <i>Xenopus</i> homolog of <i>Drosophila</i> notch", <i>Science</i> <u>249</u> :1438-1441 (1990).						
MX	Concordet, J. and P. Ingham, "Developmental biology. Patterning goes sonic", <i>Nature</i> <u>375</u> (6529):279-280 (May 1995).						

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MY	Curry, et al., "Sequence analysis reveals homology between two proteins of the flagellar radial spoke", <i>Mol. Cell. Biol.</i> 12 :3967-3977 (1992).
MZ	Davidson, E. H., "How embryos work: a comparative view of diverse modes of cell fate specification", <i>Develop.</i> 108 :365-389 (1990).
NA	Davis, A. P. and M. R. Capecchi, "Axial homeosis and appendicular skeleton defects in mice with a targeted disruption of <i>hoxd-1</i> ", <i>Devel.</i> 120 :2187-2198 (1994).
NB	Dickinson, W., "Molecules and morphology: Where's the homology", <i>TIG</i> 11 (4):119-120 (1995).
NC	Dingemans, M. A. et al., "The expression of liver-specific genes within rat embryonic hepatocytes is a discontinuous process", <i>Differentiation</i> 56 :153-162 (1994).
NL	Dollé, P. et al., "Coordinate expression of the murine <i>Hox-5</i> complex homeobox-containing genes during limb pattern formation", <i>Nature</i> 342 :767-772 (1989).
NE	Dollé, P. et al., "Disruption of the <i>Hoxd-13</i> gene induces localized heterochrony leading to mice with neotenic limbs", <i>Cell</i> 75 :431-441 (1993).
NF	Echelard, Y. et al., "Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity", <i>Cell</i> 75 :1417-1430 (1993).
NG	Ekker, S. et al., "Distinct expression and shared activities of members of the hedgehog gene family of <i>Xenopus laevis</i> ", <i>Devel.</i> 121 (8):2337-2347 (Aug. 1995).
NH	Ericson, J. et al., "Sonic hedgehog induces the differentiation of ventral forebrain neurons: a common signal for ventral patterning within the neural tube", <i>Cell</i> 81 (5):747-756 (June 1995).
NI	Ettelaie, C. et al., "The effect of lipid peroxidation and lipolysis on the ability of lipoproteins to influence thromboplastin activity", <i>Biochim. Biophys. Acta.</i> 1257 (1):25-30 (June 1995).
NJ	Fahmer, K. et al., "Transcription of <i>H-2</i> and <i>Qa</i> genes in embryonic and adult mice", <i>EMBO J.</i> 6 :1265-1271 (1987).
NK	Fallon, J. F. et al., "FGF-2: Apical ectodermal ridge growth signal for chick limb development", <i>Science</i> 264 :104-107 (1994).
NL	Fan, C. et al., "Long-range sclerotome induction by sonic hedgehog: Direct role of the amino-terminal cleavage product and modulation by the cyclic AMP signaling pathway", <i>Cell</i> 81 :457-465 (5 May 1995).
NM	Fietz, M. et al., "The hedgehog gene family in <i>Drosophila</i> and vertebrate development", <i>Devel. (Suppl.)</i> :43-51 (1994).
NN	Forbes, A. J. et al., "Genetic analysis of <i>hedgehog</i> signaling in the <i>Drosophila</i> embryo", <i>Devel.</i> 119 (Suppl.):115-124 (1993).
NO	Francis, P. H. et al., "Bone morphogenetic proteins and a signaling pathway that controls patterning in the developing chick limb", <i>Devel.</i> 120 :209-218 (1994).
NP	Gallop, M. et al., "Applications of combinatorial technologies to drug discovery. 1. Background and peptide combinatorial libraries", <i>J. Med. Chem.</i> 37 (9):1233-1251 (1994).
NQ	Gérard, M. et al., "Structure and activity of regulatory elements involved in the activation of the <i>Hoxd-11</i> gene during late gastrulation", <i>EMBO J.</i> 12 :3539-3550 (1993).
NR	Gurdon, J. B., "The generation of diversity and pattern in animal development", <i>Cell</i> 68 :185-199 (1992).
NS	Gustin, et al., "Characterization of the Role of Individual Protein Binding Motifs Within the Hepatitis B Virus Enhancer 1 on X Promoter Activity Using Linker Scanning Mutagenesis", <i>Virology</i> 193 : 653-660 (1993).
NT	Hall, T. et al., "A potential catalytic site revealed by the 1.7-Å crystal structure of the amino-terminal signaling domain of sonic hedgehog", <i>Nature</i> 378 (6553):212-216 (Nov 1995).
NU	Halpern, M. E. "Induction of Muscle Pioneers and Floor Plate is Distinguished by the Zebrafish no tail Mutation", <i>Cell</i> 75 : 99-111 (1993).
NV	Hamburger, V. and H. L. Hamilton, "A series of normal stages in the development of the chick embryo", <i>J. Morph.</i> 88 :49-92 (1951).
NW	Hammerschmidt, M. et al., "The world according to hedgehog", <i>TIG</i> 13 (1):14-21 (1997).

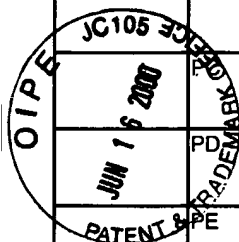


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	NX	Haramis, A. et al., "The limb deformity mutation disrupts the SHH/ FGF-4 feedback loop and regulation of 5' <i>HoxD</i> genes during limb pattern formation", <i>Devel.</i> <u>121</u> (12):4161-4170 (Dec. 1995).
	NY	Hardy, A. et al., "Gene expression, polarising activity and skeletal patterning in reaggregated hind limb mesenchyme", <i>Devel.</i> <u>121</u> (12):4329-4337 (Dec. 1995).
	NZ	Harmon, C. S. et al., "Evidence that activation of protein kinase A inhibits human hair follicle growth and hair fibre production in organ culture and DNA synthesis in human and mouse hair follicle organ culture", <i>British J. Dermatol.</i> <u>136</u> :853-858 (1997).
	OA	Hatta, K. et al., "The cyclops mutation blocks specification of the floor plate of the zebrafish central nervous system", <i>Nature</i> <u>350</u> :339-341 (1991).
	OB	Heberlein, U. et al., "The TGB β homolog <i>dpp</i> and the segment polarity gene <i>hedgehog</i> are required for propagation of a morphogenetic wave in the <i>Drosophila</i> retina", <i>Cell</i> <u>75</u> :913-926 (1993).
	OC	Heemskerk, J. and S. DiNardo, " <i>Drosophila hedgehog</i> acts as a morphogen in cellular patterning", <i>Cell</i> <u>76</u> :449-460 (1994).
	OD	Hidalgo, A. and P. Ingham, "Cell patterning in the <i>Drosophila</i> segment: spatial regulation of the segment polarity gene <i>patched</i> ", <i>Devel.</i> <u>110</u> :291-301 (1990).
	OE	Hooper, J. and M. Scott, "The <i>Drosophila patched</i> gene encodes a putative membrane protein required for segmental patterning", <i>Cell</i> <u>59</u> :751-765 (1989).
	OF	Hynes, R. O., "Integrins: A family of cell surface receptors", <i>Cell</i> <u>48</u> :549-554 (1987).
	OG	Ingham, P. W., "Signaling by hedgehog family proteins in <i>Drosophila</i> and vertebrate development", <i>Curr. Opin. Genet. Dev.</i> <u>5</u> (4):478-484 (Aug 1995).
	OH	Ingham, P. W., "Hedgehog points the way", <i>Current Biology</i> <u>4</u> (4):347-350 (1994).
	OI	Ingham, P. W., "Localized <i>Hedgehog</i> activity controls spatial limits of wingless transcription in the <i>Drosophila</i> embryo", <i>Nature</i> <u>366</u> :560-562 (1993).
	OJ	Ingham, P. W. and A. Hidalgo, "Regulation of wingless transcription in the <i>Drosophila</i> embryo", <i>Devel.</i> <u>117</u> :283-291 (1993).
	OK	Ingham, P. W. et al., "Role of the <i>Drosophila patched</i> gene in positional signaling", <i>Nature</i> <u>353</u> :184-187 (1991).
	OL	Izpisua-Belmonte, J. -C. et al., "Expression of the homeobox <i>Hox-4</i> genes and the specification of position in chick wing development", <i>Nature</i> <u>350</u> :585-589 (1991).
	OM	Izpisua-Belmonte, J. -C. et al., "Expression of <i>Hox-4</i> genes in the chick wings links pattern formation to the epithelial- mesenchymal interaction that mediate growth", <i>EMBO J.</i> <u>11</u> :1451-1457 (1992).
	ON	Jiang, J. and G. Struhl, "Protein kinase A and hedgehog signaling in <i>Drosophila</i> limb development", <i>Cell</i> <u>80</u> (4):563-572 (Feb. 1995).
	OO	Jessel, T. M. and D. A. Melton, "Diffusible factors in vertebrate embryonic induction", <i>Cell</i> <u>68</u> :257-270 (1992).
	OP	Johnson, R. L. and C. Tabin, "The long and short of hedgehog signaling", <i>Cell</i> <u>81</u> :313-315 (5 May 1995).
	OQ	Johnson, R. L. et al., "Patched overexpression alters wing disc size and pattern: transcriptional and post-transcriptional effects on hedgehog targets", <i>Devel.</i> <u>121</u> (12):4237-4245 (Dec. 1995).
	OR	Johnson, R. L. et al., "Ectopic expression of sonic hedgehog alters dorsal-ventral patterning of somites", <i>Cell</i> <u>79</u> (7):1165-1173 (Dec. 1994).
	OS	Johnson, R. L. et al., "Mechanism of limb patterning", <i>Curr. Opin. Genet. Dev.</i> <u>4</u> (4):535-542 (Aug. 1994).
	OT	Johnson, R. L. et al., "Sonic hedgehog: a key mediator of anterior-posterior patterning of the limb and dorso-ventral patterning of axial embryonic structures" <i>Biochem. Soc. Trans.</i> <u>22</u> (3):569-574 (Aug. 1994).
	OU	Jones, M. et al., "Involvement of bone morphogenetic protein-4 (BMP-4) and Vgr-1 in morphogenesis and neurogenesis in the mouse", <i>Devel.</i> <u>111</u> :531-542 (1991).
	OV	Kalderon, D., "Morphogenetic signalling. Responses to hedgehog" <i>Curr. Biol.</i> <u>5</u> (6):580-582 (June 1995).

OW	Koonin, E., "A protein splice-junction motif in hedgehog family proteins", <i>Trends Biochem. Sci.</i> <u>20</u> (4):141-142 (April 1995).
OX	Kornblihtt, A. R. et al., "Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene", <i>EMBO J.</i> <u>4</u> :1755-1759 (1985).
OY	Kornfeld, R. and S. Kornfeld, "Assembly of asparagine-linked oligosaccharides", <i>Ann. Rev. Biochem.</i> <u>54</u> :631-664(1985).
OZ	Krauss, S. et al., "Expression of the zebrafish paired box gene <i>pax[<i>zf-b</i>]</i> during early neurogenesis", <i>Devel.</i> <u>113</u> :1193-1206 (1991).
PA	Krauss, S. et al., "A functionally conserved homolog of the Drosophila Segment polarity gene <i>hh</i> is expressed in tissues with polarizing activity in zebrafish embryos", <i>Cell</i> <u>75</u> :1431-1444 (1993).
PB	Lai, C. et al., "Patterning of the neural ectoderm of <i>Xenopus laevis</i> by the amino-terminal product of hedgehog autoproteolytic cleavage", <i>Devel.</i> <u>121</u> :2349-2360 (1995).
PC	Laufer, E. et al., "Sonic hedgehog and <i>Fgf-4</i> act through a signaling cascade and feedback loop to integrate growth and patterning of the developing limb bud", <i>Cell</i> <u>79</u> :993-1003 (16 Dec.1994).
PD	Lee, J. J. et al., "Secretion and localized transcription suggest a role in positional signaling for products of the segmentation gene <i>hedgehog</i> ", <i>Cell</i> <u>71</u> :33-50 (1992).
PE	Lee, J. J. et al., "Autoproteolysis in hedgehog protein biogenesis", <i>Science</i> <u>266</u> (5190):1528-1537 (Dec. 1994).
PF	Lee, S. J. "Expression of growth/ differentiation factor1 in the nervous system: Conservation of a bicistronic structure", <i>Proc. Natl. Acad. Sci. USA</i> <u>88</u> :4250-4254 (Year).
PG	Levin, M. et al., "A molecular pathway determining left-right asymmetry in chick embryogenesis", <i>Cell</i> <u>82</u> (5):803-814 (Sept. 8, 1995).
PH	Li, W. et al., "Function of protein kinase A in hedgehog signal transduction and drosophila imaginal disc development", <i>Cell</i> <u>80</u> (4):553-562(Feb. 1995).
PI	Lopez-Martinez, A. et al., "Limb-patterning activity and restricted posterior localization of the amino-terminal product of sonic hedgehog cleavage", <i>Curr. Biol.</i> <u>5</u> (7):791-796 (July 1995).
PJ	Lumsden, A. and A. Graham, "Neural patterning: A forward role for hedgehog", <i>Curr. Biol.</i> <u>5</u> (12):1347-1350 (Dec. 1995).
PK	Ma, C. et al., "Molecular cloning and characterization of rKik10, a cDNA encoding T-kininogenase from rat submandibular gland and kidney", <i>Biochem.</i> <u>31</u> (44):10922-10928 (1992).
PL	Ma, C. et al., "The segment polarity gene <i>hedgehog</i> is required for the progression of the morphogenetic furrow in the developing Drosophila eye", <i>Cell</i> <u>75</u> :927-938 (1993).
PM	Ma, C. and K. Moses, " <i>Wingless</i> and <i>patched</i> are negative regulators of the morphogenetic furrow and can affect tissue polarity in the developing Drosophila compound eye", <i>Devel.</i> <u>121</u> (8):2279-2289 (Aug. 1995).
PN	Marigo, V. et al., "Biochemical evidence that <i>patched</i> is the hedgehog receptor", <i>Nature</i> <u>384</u> :176-179 (1996).
PO	Maccabe, J. A. and B. W. Parker, "The target tissue of limb-bud polarizing activity in the induction of supernumerary structures", <i>J. Embryol. Exp. Morph.</i> <u>53</u> :67-73 (1979).
PP	Maiese, K. et al., "Protein kinases modulate the sensitivity of hippocampal neurons to nitric oxide toxicity and anoxia", <i>J. Neurosci. Res.</i> <u>36</u> :77-87 (1993).
PQ	Marti, E. et al., "Distribution of Sonic hedgehog peptides in the developing chick and mouse embryo", <i>Devel.</i> <u>121</u> (8):2537-2547 (Aug. 1995).
PR	Marti, E. et al., "Requirement of 19K form of Sonic hedgehog for induction of distinct ventral cell types in CNS explants", <i>Nature</i> <u>375</u> (6529):322-325 (May 1995).
PS	Mavillio, F. et al. "Activation of four homeobox gene clusters in human embryonal carcinoma cells induced to differentiate by retinoic acid", <i>Differentiation</i> <u>37</u> :73-79 (1988).
PT	McGinnis, W. and R. Krumlauf, "Homeobox genes and axial patterning", <i>Cell</i> <u>68</u> :283-302 (1992).
PU	Mohler, J., "Requirements for <i>hedgehog</i> , a segmental polarity gene, in patterning larval and adult cuticle of drosophila", <i>Genetics</i> <u>120</u> :1061-1072 (1988).



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PV	Mohler, J. and K. Vani, "Molecular organization and embryonic expression of the <i>hedgehog</i> gene involved in cell-cell communication in segmental patterning of <i>Drosophila</i> ", <i>Devel.</i> <u>115</u> :957-971 (1992).
PW	Morgan, B. A. et al., "Targeted misexpression of <i>Hox-4.6</i> in the avian limb bud causes apparent homeotic transformations", <i>Nature</i> <u>358</u> :236-239 (1992).
PX	Nakano, Y. et al., "A protein with several possible membrane-spanning domains encoded by the <i>Drosophila</i> segment polarity gene <i>patched</i> ", <i>Nature</i> <u>341</u> :508-513 (1989).
PY	Ngo, J. et al., "Computational Complexity Protein", Merz and LeGrand, ed. @ Birkhouse Boston (1994).
PZ	Niswander, L. and G. R. Martin, "FGF-4 and BMP-2 have opposite effects on limb growth", <i>Nature</i> <u>361</u> :68-71(1993).
QA	Niswander, L. et al., "A positive feedback loop coordinates growth and patterning in the vertebrate limb", <i>Nature</i> , <u>371</u> :609-612 (October 1994).
QB	Nohno, T. et al., "Involvement of the Chox-4 Chicken Homeobox Genes in Determination of Anteroposterior Axial Polarity during Limb Development", <i>Cell</i> , Vol. <u>64</u> : 1197- 1205 (March 22, 1991).
QC	Nohno, T. et al., "Involvement of the Sonic hedgehog gene in chick feather formation", <i>Biochem. Biophys. Res. Comm.</i> <u>206</u> (1): 33-39 (Jan. 1995).
QD	O'Farrell, P. H., "Unanimity waits in the wings", <i>Nature</i> <u>368</u> :188-189 (1994).
QE	Parisi, M. J. et al., "The role of the hedgehog/patched signaling pathway in epithelial stem cell proliferation: From fly to human", <i>Cell Res.</i> <u>8</u> :15-21 (1998).
QF	Parr, B. A. et al., "Mouse Wnt genes exhibit discrete domains of expression in the early embryonic CNS and limb buds", <i>Development</i> <u>119</u> :247-261 (1993).
QG	Patel, N. H. et al., "The role of segment polarity genes during <i>Drosophila</i> neurogenesis", <i>Genes & Devel.</i> <u>3</u> :890-904 (1989).
QH	Peifer, M., "The two faces of hedgehog", <i>Science</i> <u>266</u> (5190):1492-1493 (Dec. 1994).
QI	Perrimon, N. et al., "Generating lineage-specific markers to study <i>Drosophila</i> development", <i>Develop. Genet.</i> , <u>12</u> :238-252 (1991).
QJ	Perrimon, N., "Hedgehog and beyond", <i>Cell</i> <u>80</u> :517-520 (24 Feb. 1995).
QK	Pham, A. et al., "The Suppressor of <i>fused</i> gene encodes a novel PEST protein involved in <i>Drosophila</i> segment polarity establishment" <i>Genetics</i> <u>140</u> (2):587-598 (June 1995).
QL	Phillis, J. W. and M. H. O'Regan, "Mechanisms of glutamate and aspartate release in the ischemic rat cerebral cortex", <i>Brain Res.</i> <u>730</u> :150-164 (1996).
QM	Placzek, M. et al., "Induction of floor plate differentiation by contact-dependent, homeogenetic signals", <i>Development</i> <u>117</u> : 205 218 (1993).
QN	Placzek, M. et al., " Orientation of Commissural Axons <i>in vitro</i> in response to a floor plate-derived chemoattractant", <i>Develop.</i> <u>110</u> :19-30 (1990).
QO	Pollock, R. A. et al., "Altering the boundaries of <i>Hox3.1</i> expression: Evidence for antipodal gene regulation", <i>Cell</i> <u>71</u> :911-923 (1992).
QP	Porter, J. et al., "The product of hedgehog autoproteolytic cleavage active in local and long-range signalling", <i>Nature</i> <u>374</u> (6520):363-366 (23 March 1995).
QQ	Reeck, et al., "'Homology' in proteins and nucleic acids: A terminology muddle and a way out of it", <i>Cell</i> <u>50</u> :667 (28 Aug. 1987).
QR	Rennie, J., "Super Sonic", <i>Sci. Amer.</i> p.20, (April 1994).
QS	Riddle, R. D. et al., "Sonic hedgehog mediates the polarizing activity of the ZPA", <i>Cell</i> <u>75</u> :1401-1416, (31 Dec. 1993).
QT	Riddle, R. D. et al. "Induction of the LIM homeobox gene <i>Lmx1</i> by WNT7a establishes dorsoventral pattern in the vertebrate limb", <i>Cell</i> <u>83</u> :631-640 (17 Nov. 1995).

QU	Riley, B. B. et al., "Retroviral expression of FGF-2 (bFGF) affects patterning in chick limb bud", <i>Develop.</i> <u>118</u> :95-104 (1993).
QV	Roberts, D. et al., "Sonic hedgehog is an endodermal signal inducing Bmp-4 and Hox genes during induction and regionalization of the chick hindgut", <i>Develop.</i> <u>121</u> (10):3163-3174 (Oct. 1995).
QW	Roelink, H. et al., "Floor plate and motor neuron induction vhh-1, a vertebrate homolog of hedgehog expressed by the notochord", <i>Cell</i> <u>76</u> :761-775 (25 Feb. 1994).
QX	Roelink, H. et al., "Floor plate and motor neuron induction by different concentrations of the amino-terminal cleavage product of sonic hedgehog autoproteolysis", <i>Cell</i> <u>81</u> :445-455 (5 May 1995).
QY	Sachiko, I. et al., "Sonic hedgehog is expressed in epithelial cells during development of whisker, hair and tooth", <i>Biochem. Biophys. Res. Commun.</i> <u>218</u> :688-693 (1996).
QZ	Satoh, S. et al., "Neuroprotective properties of a protein kinase inhibitor against ischaemia-induced neuronal damage in rats and gerbils", <i>Br. J. Pharmacol.</i> <u>118</u> :1592-1596 (1996).
RA	St. Jacques, B. et al., "Sonic hedgehog signaling is essential for hair development", <i>Curr. Biol.</i> <u>8</u> :1058-1068 (1998).
RB	Sasaki, H. and B. L. M. Hogan, "Differential expression of multiple fork head related genes during gastrulation and axial pattern formation in the mouse embryo", <i>Develop.</i> <u>118</u> :47-59 (1993).
RC	Savage, M. et al., "Distribution of FGF- 2 suggests it has a role in chick limb bud growth", <i>Devel. Dynamics</i> <u>198</u> :159-170 (1993).
RD	Schuske, K. et al., " <i>Patched</i> overexpression causes loss of <i>wingless</i> expression in drosophila embryos", <i>Devel. Biol.</i> <u>164</u> : 300-311 (1994).
RE	Smith, J. C., "Hedgehog, the floor plate, and the zone of polarizing activity", <i>Cell</i> <u>76</u> :193-196 (1994).
RF	Stachel, S. E. et al., "Lithium perturbation and goosecoid expression identify a dorsal specification pathway in the pregastrula zebrafish", <i>Develop.</i> <u>117</u> :1261-1274 (1993).
RG	Stolow, M. and Shi, Y., "Xenopus sonic hedgehog as a potential morphogen during embryogenesis and thyroid hormone-dependent metamorphosis", <i>Nucl. Acids Res.</i> <u>23</u> (13):2555-2562 (1995).
RH	Tabata, T. and T. B. Kornberg, " Hedgehog is a signaling protein with a key role in patterning drosophila imaginal discs", <i>Cell</i> <u>76</u> : 89-102 (1994).
RI	Tabata, T. et al., "The <i>Drosophila hedgehog</i> gene is expressed specifically in posterior compartment cells and is a target of engrailed regulation", <i>Genes & Develop.</i> <u>6</u> :2635-2645 (1992).
RJ	Tabin, C. J., "Retinoids homeoboxes, and growth factors: Toward molecular models for limb development", <i>Cell</i> <u>66</u> :199-217 (26 July 1991).
RK	Tanabe, Y. et al., "Induction of motor neurons by sonic hedgehog is independent of floor plate differentiation", <i>Curr. Biol.</i> <u>5</u> (6):651-658 (June 1995).
RL	Tanaka, E. and A. Gann, "Limb development : The budding role of FGF", <i>Curr. Biol.</i> <u>5</u> (6):594- 597 (June 1995).
RM	Tashiro, S. et al. "Structure and expression of <i>hedgehog</i> , a <i>Drosophila</i> segment-polarity gene required for cell-cell communication", <i>Gene</i> <u>124</u> :183-189 (1993).
RN	Taylor, A. M. et al., "Contrasting distributions of <i>patched</i> and <i>hedgehog</i> proteins in the <i>Drosophila</i> embryo", <i>Mech. Develop.</i> <u>42</u> : 89-96 (1993).
RO	Thaller, C. and G. Eichele, " Identification and spatial distribution of retinoids in the developing chick limb bud", <i>Nature</i> <u>327</u> : 625-628 (1987).
RP	Thummel, et al., "Vectors for <i>Drosophila</i> P-element-mediated transformation and tissue culture transfection", <i>Gene</i> <u>74</u> :445-456 (1988).
RQ	Tickle, C. et al., "A quantitative analysis of the effect of all-trans-retinoic acid on the pattern of chick wing development", <i>Develop. Biol.</i> <u>109</u> :82-95 (1985).
RR	Tickle, C. et al., "Vertebrate limb development", <i>Curr. Opin. Genet. Dev.</i> <u>5</u> (4):478-484 (1995).
RS	Tickle, C. and G. Eichele, "Vertebrate limb development", <i>Ann. Rev. Cell Biol.</i> <u>10</u> :121-152 (1994).

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RT	Van Straaten, H. W. M. et al. "Effect of the notochord on the differentiation of a floor plate area in the neural tube of the chick embryo", <i>Anat. Embryol.</i> <u>177</u> :317-324 (1988).
RU	Vogel, A. and C. Tickle, "FGF-4 maintains polarizing activity of posterior limb bud cells <i>in vivo</i> and <i>in vitro</i> ", <i>Develop.</i> <u>119</u> :199- 206 (1993).
RV	Wallace, et al., "Oligonucleotide probes for the screening of recombinant DNA libraries", <i>Methods in Enzymol.</i> <u>152</u> :432-443 (1987).
RW	Wanek, N. t al., "Conversion by retinoic acid of anterior cells into ZPA cells in the chick wing bud", <i>Nature</i> <u>350</u> :81-83 (7 March 1991).
RX	Yamada, T. et al., "Control of cell pattern in the developing nervous system: Polarizing activity of the floor plate and notochord", <i>Cell</i> , <u>64</u> :635-647, (8 Feb. 1991).
RY	Yang, Y. and L. Niswander, "Interaction between the signaling molecules WNTZ7a and SHH during vertebrate limb development: dorsal signals regulate anteroposterior patterning", <i>Cell</i> <u>80</u> :939-947 (24 March 1995).
RZ	Yun-Bo Shi, "Cell-cell and cell ECM interactions in epithelial apoptosis and cell renewal during frog intestinal development", <i>Cell Biochem. Biophys.</i> <u>27</u> :179-202 (1995).
SA	Zappavigna, et al., "Hox4 genes encode transcription factors with potential auto- and cross-regulatory capacities ", <i>EMBO J.</i> <u>10</u> (13):4177-4187 (1991).
SB	Zardoya, et al., "Evolution and orthology of hedgehog genes", <i>TIG</i> <u>12</u> (12):496-497 (1996)
SC	Zecca, M. et al., "Sequential organizing activities of <i>engrailed</i> , <i>hedgehog</i> and <i>decapentaplegic</i> in the <i>Drosophila</i> wing", <i>Dev.</i> <u>121</u> :2265-2278 (Aug. 1995).

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